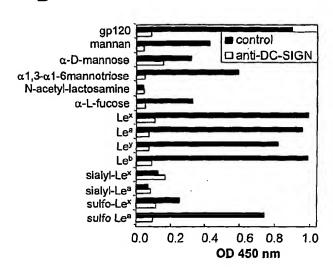
Fig. 1

A Is table of structures

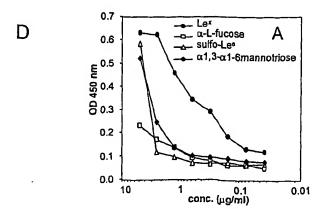
В





Le x

LDNF

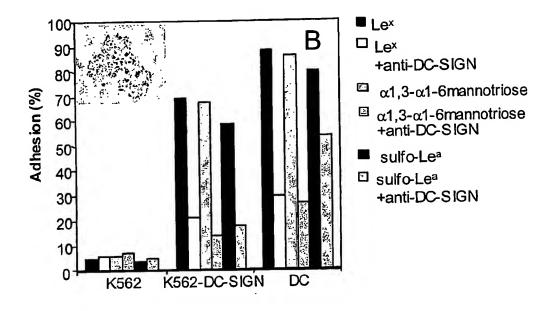


gp120

0,2

BEST AVAILABLE COPY

Fig. 2



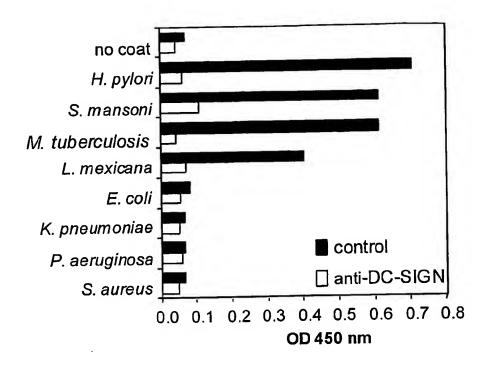


Fig. 3A

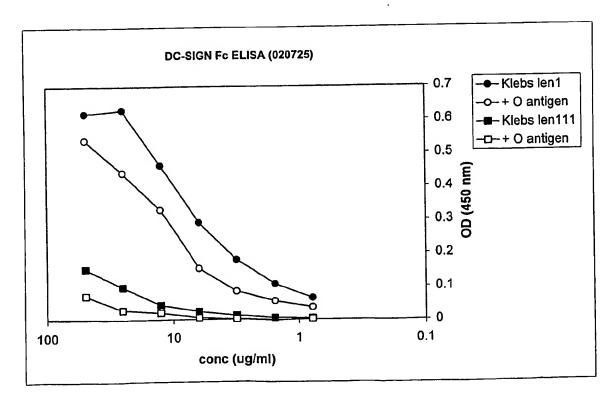


Fig. 3B

Fig. 4

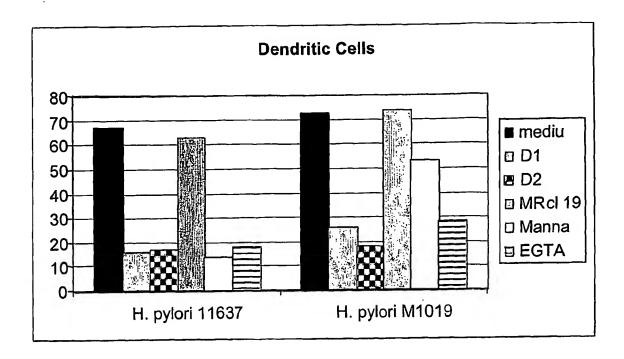


Fig. 5

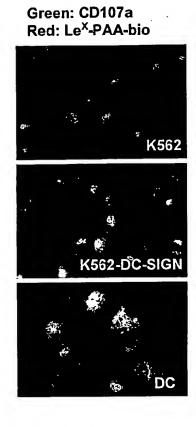


Fig. 6

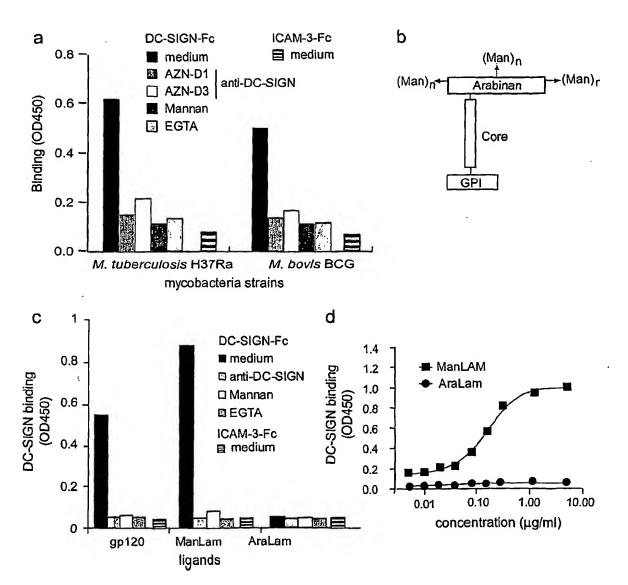
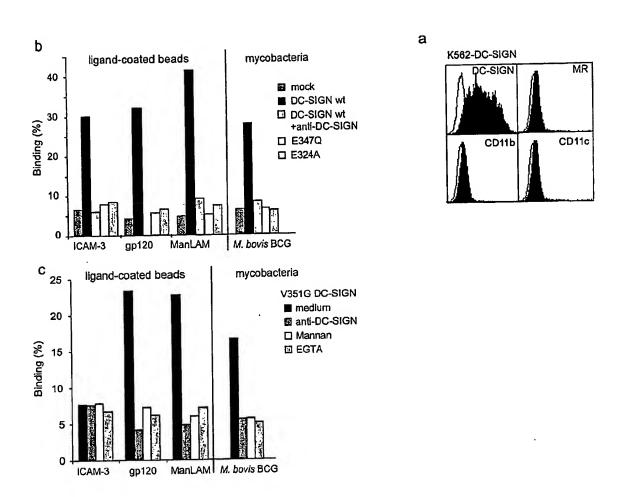


Fig. 7



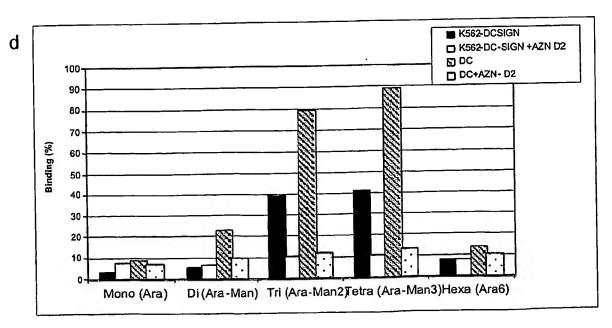
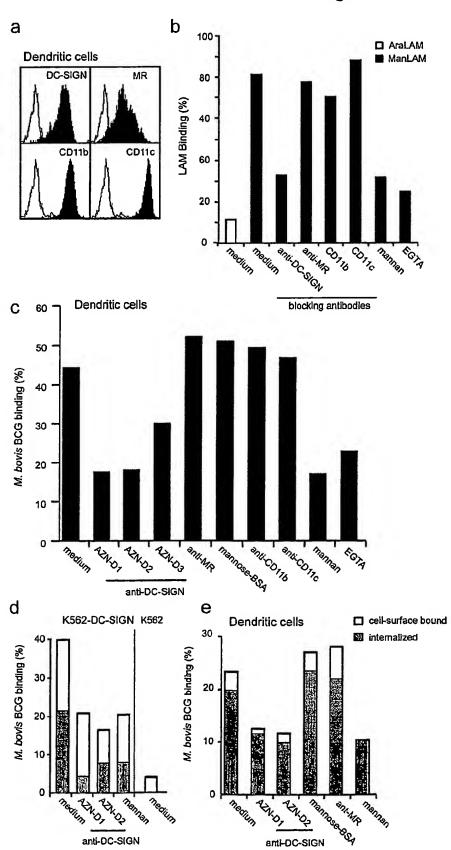
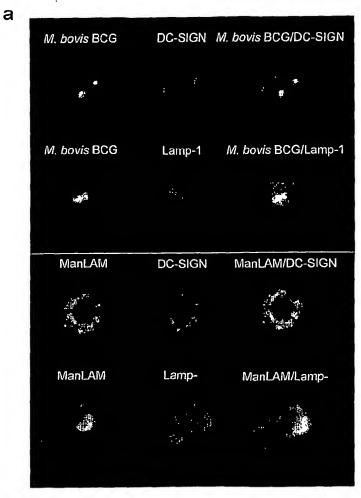


Fig. 8



SUBSTITUTE SHEET (RIJI F 26)

Fig. 9



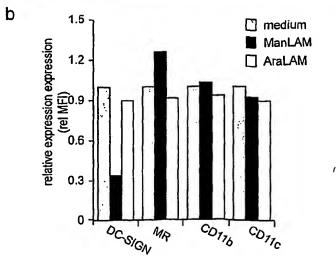
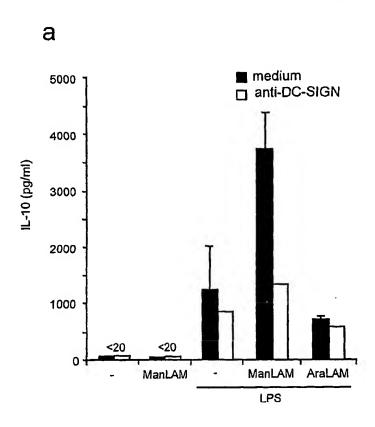


Fig. 10



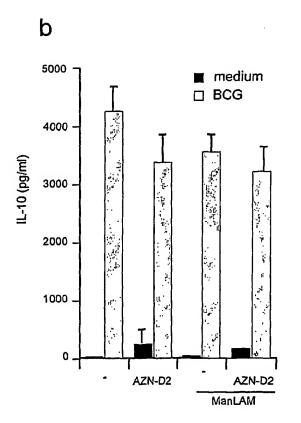


Fig. 11

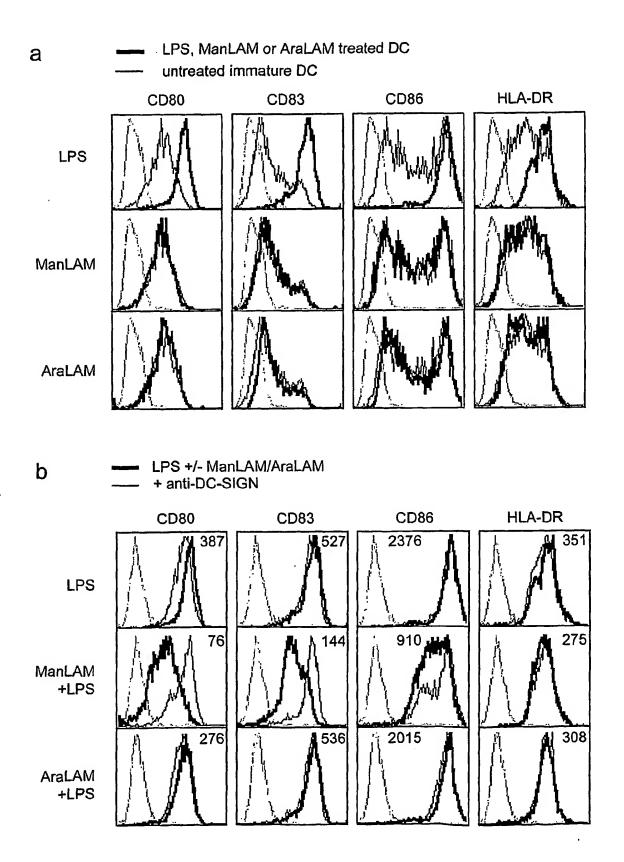
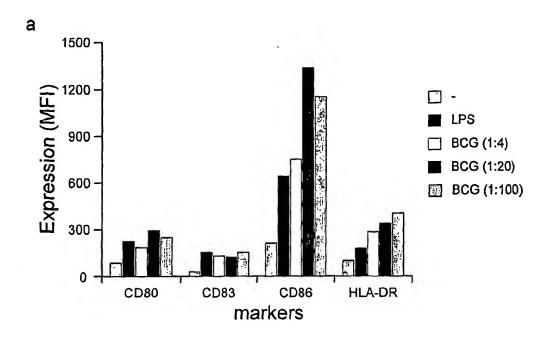


Fig. 12



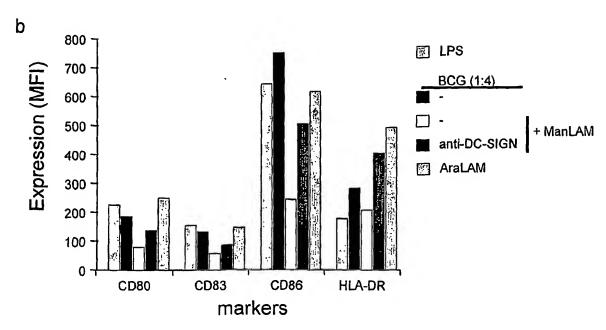


Fig. 13

Carbohydrate antigens on S. mansoni SEA

Carbohydrate epitope	Shortname	anti-glycan MAb	
	Lewis-X	CB10 (32)	
<u> </u>	LDN	SMLDN1.1 (31)	
$ \begin{array}{c} $	LDNF	SMLDNF1 (4)	
α3	LDN-DF	114-5B1-A (12)	
Gal Gi	cNAc G	alNAc 🛆 Fucose	

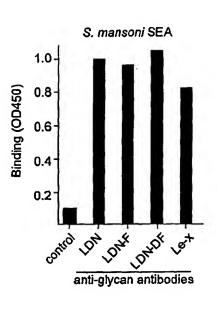
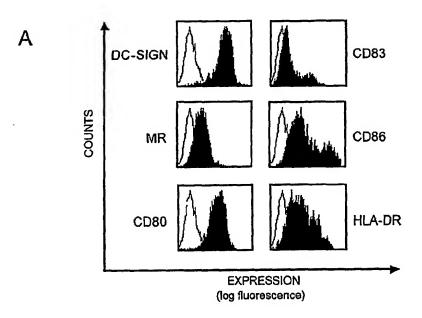


Fig. 14



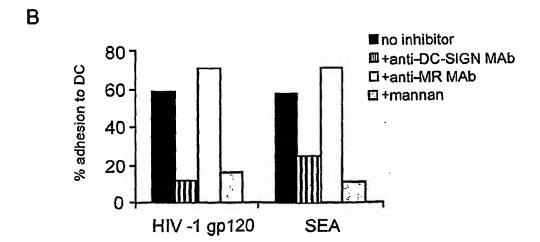


Fig. 15

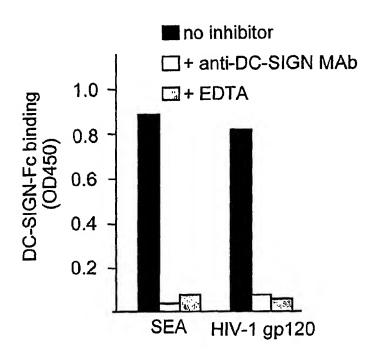


Fig. 16

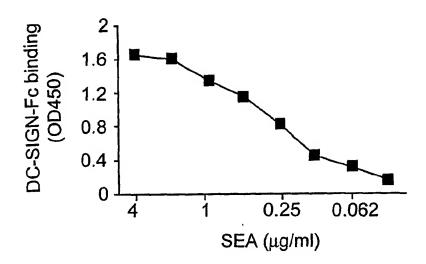
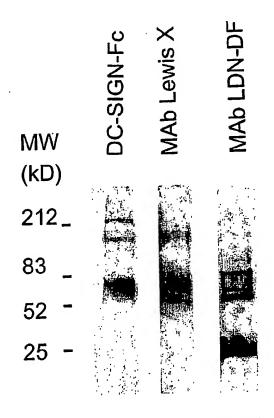
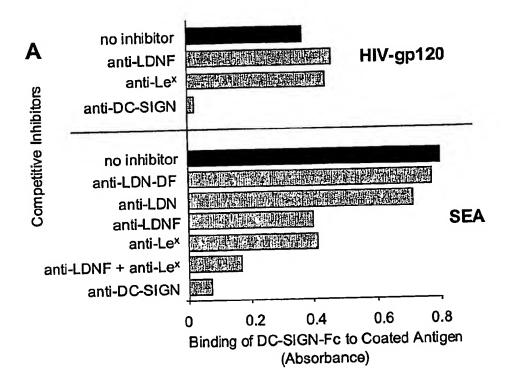


Fig. 17



S. mansoni SEA

Fig. 18



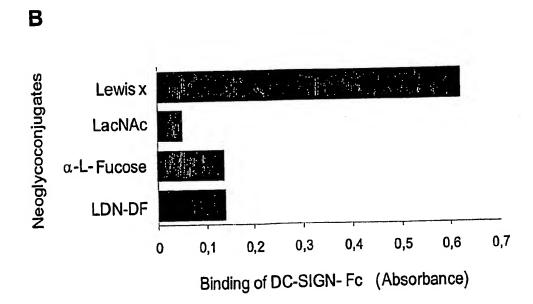
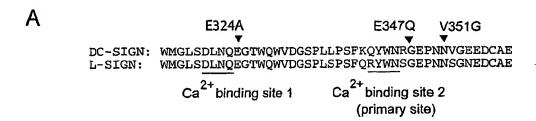
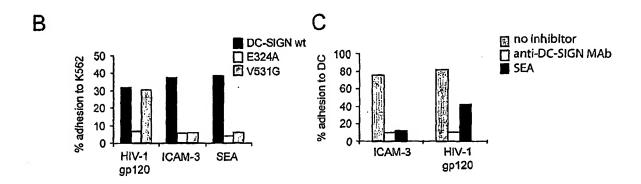


Fig. 19





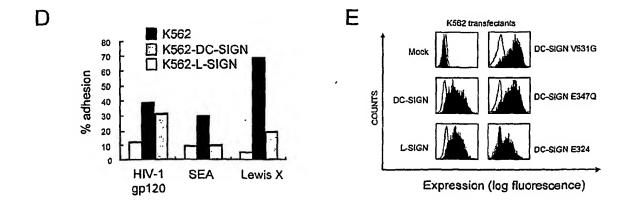


Fig. 20A

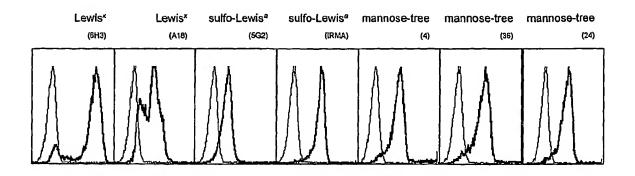


Fig. 20B

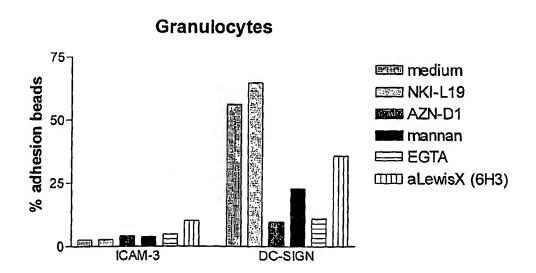
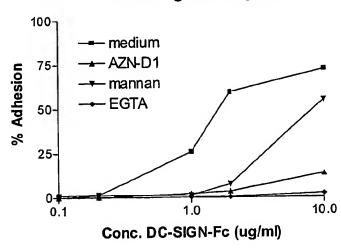


Fig. 21

Titration granulocytes



Granulocytes

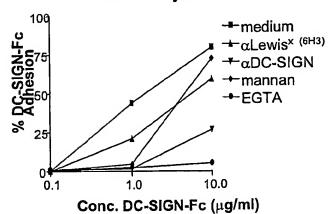


Fig. 22A

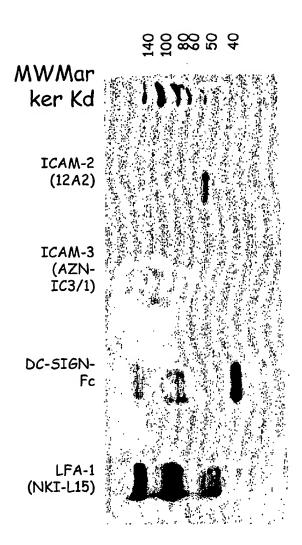


Fig. 22B

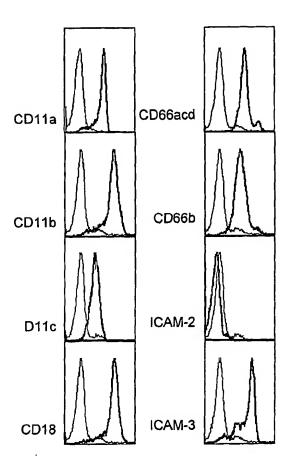
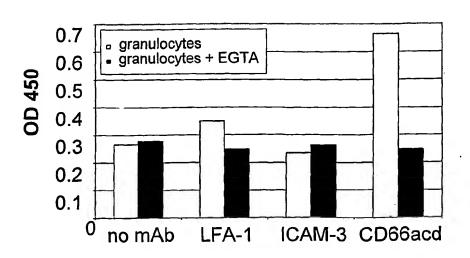
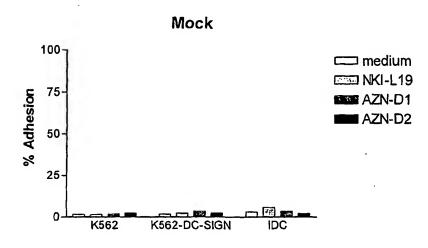


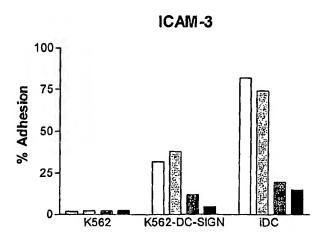
Fig. 22C



SUBSTITUTE SHFFT (RIII F 26)

Fig. 23





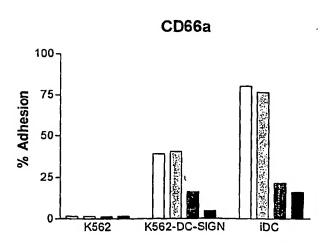


Fig. 24

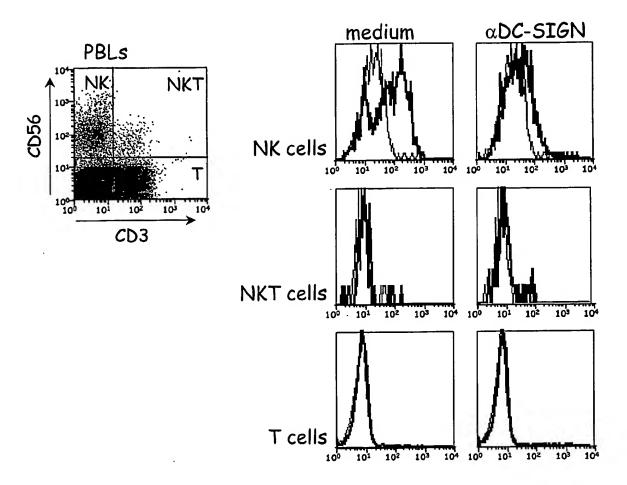


Fig. 25

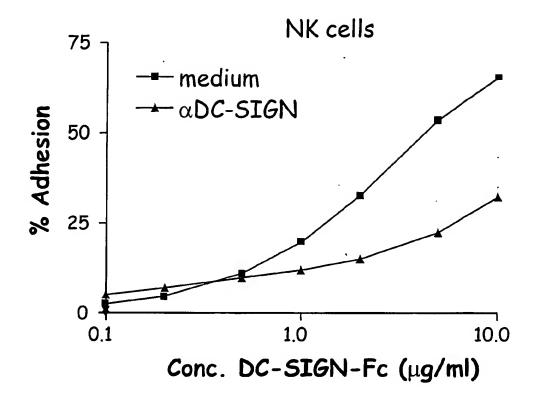


Fig. 26

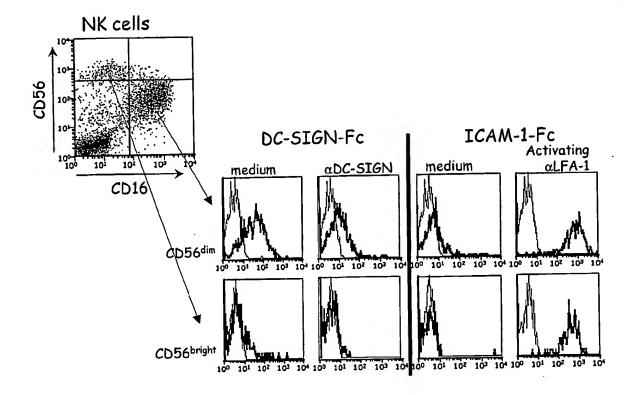
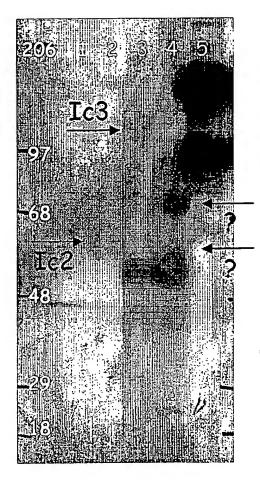


Fig. 27



- 1. control
- 2. ICAM-2
- 3. ICAM-3
- 4. DC-SIGN ligand
- 5. LFA-1

→ DC-SIGN binds
ICAM-2? and 75
kD ligand on NK
cells

Fig. 28

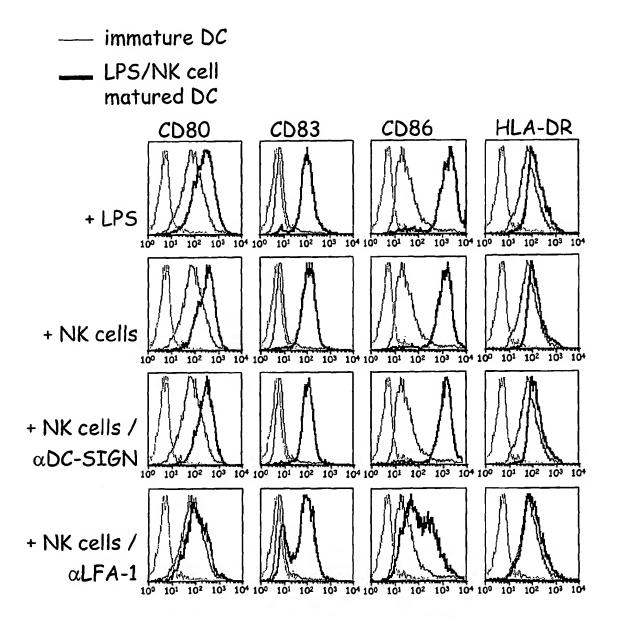
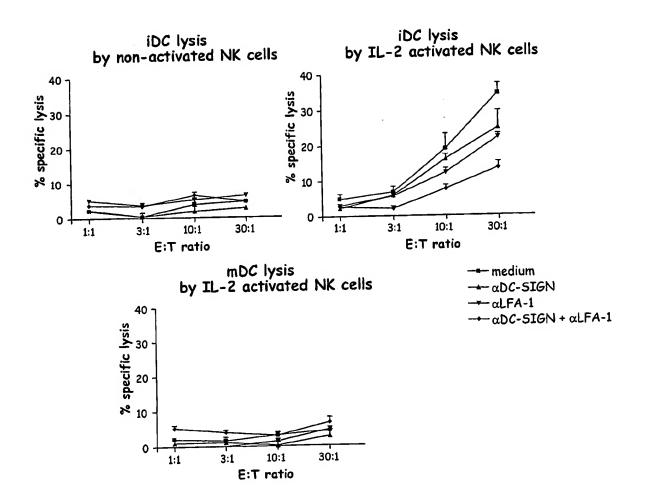


Fig. 29



WO 2004/041292

30/77

Fig. 30

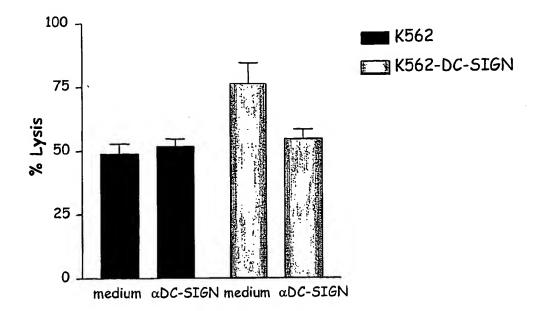
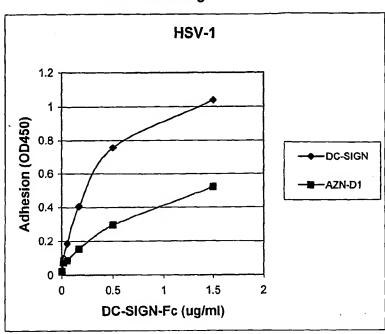


Fig. 31

HSV-1 binding



HSV-2 binding

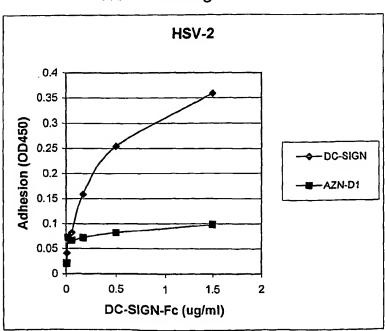
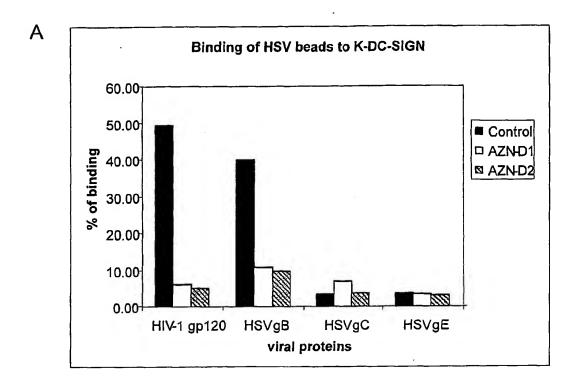


Fig. 32



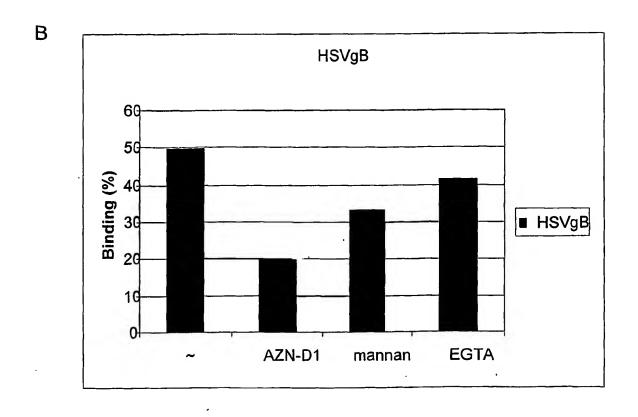


Fig. 33A

mSIGNR1 binds mannose-containing carbohydrates, similar to DC-SIGN and L-SIGN

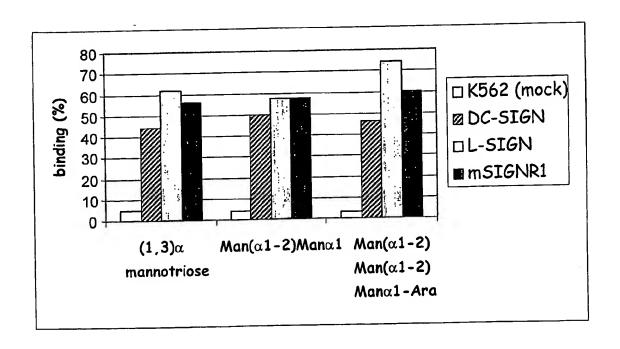


Fig. 33B

DC-SIGN, L-SIGN and mSIGNR1 bind differently to Lewis antigens

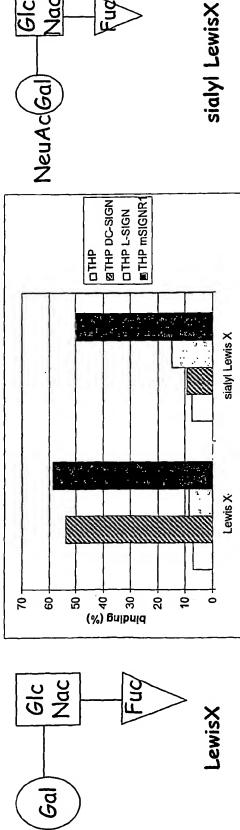


Fig. 33C

Carbohydrate specificity of DC-SIGN, L-SIGN and mSIGNR1

	DC-SIGN	L-SIGN	mSIGNR1
LewisX	+	\bigcirc	+
sialyl LewisX		-	+
sulfo LewisX	+	\bigcirc	+
LewisY	+	+	+
LewisA	+	+	+
sialyl LewisA	-	-	+
sulfo LewisA	+	+	+
LewisB	+	+	+

Fig. 34

pathogens with mannose-containing carbohydrates bind mSIGNR1

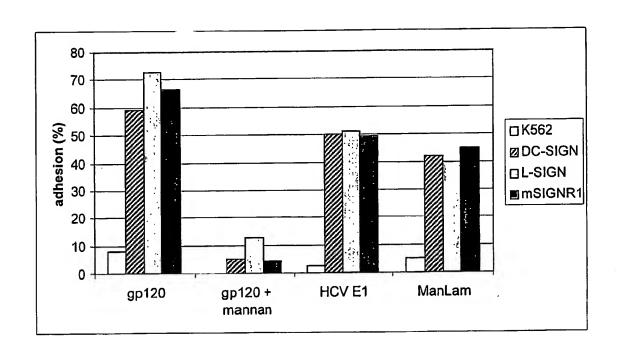


Fig. 35

DC-SIGN-Fc binds HCV-envelope proteins

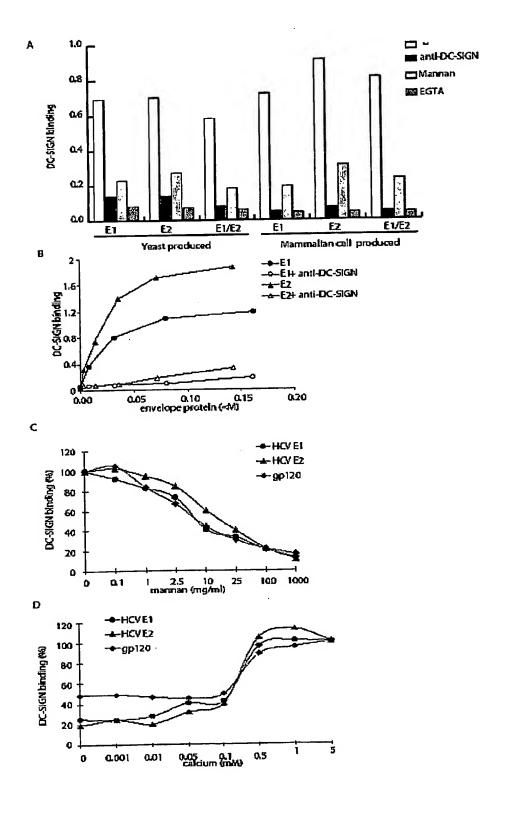
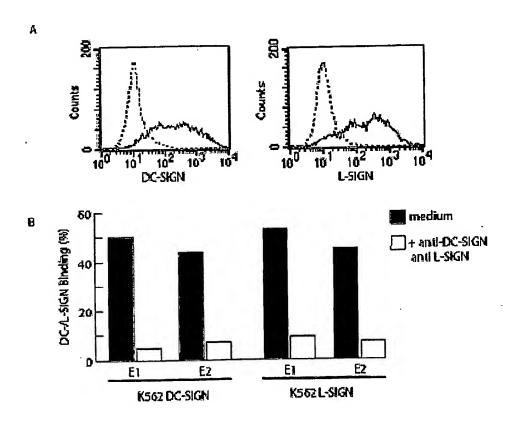


Fig. 36

Cellular DC-SIGN and L-SIGN bind HCV E1 and E2 proteins

DC-SIGN has similar binding site for gp120 and HCV



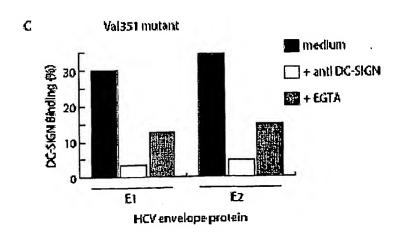


Fig. 36D

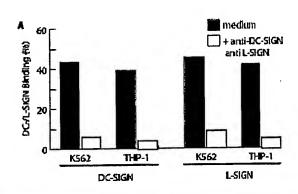
Essential amino acid residues in DC-SIGN binding to its ligands gp120 and HCV envelope proteins

DC-SIGN mutant				
DO-SIGIV mutant	gp120	HCV E1	HCV E2	HCV E1/E2
Wild type	% 45	% 50	% 45	% 50
E347Q N349D N365D	4 0 0		gand 7 nding 9	. 7 7 9
D366A	3	4 si	Ca ²⁺ ite 2	6
D320A E324A N350A D355A	7 0 1 2		Ca ²⁺ 7 ite 1 8 8	5 6 5

Stable K562 transfectamts

Fig. 37

HCV is internalized by DC-SIGN and L-SIGN; internalization pathway depends on cell-line



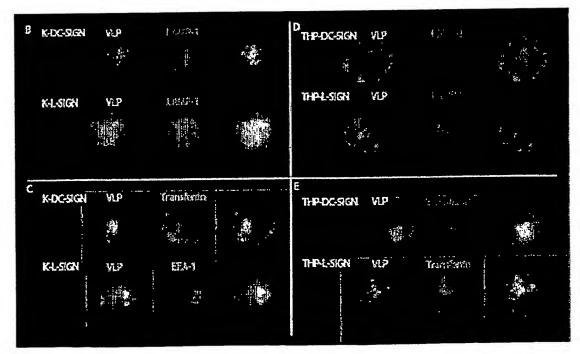


Fig. 38

Immature and mature DC bind HCV via DC-SIGN

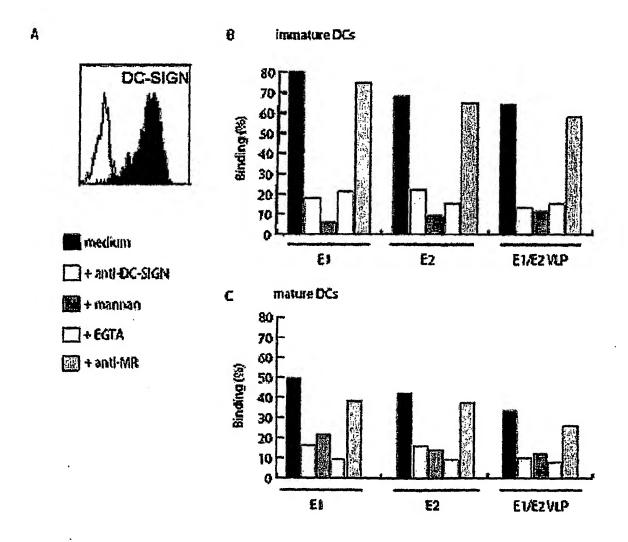


Fig. 39

Immature DC capture and internalize HCV through DC-SIGN; HCV is targeted to the early endosomes

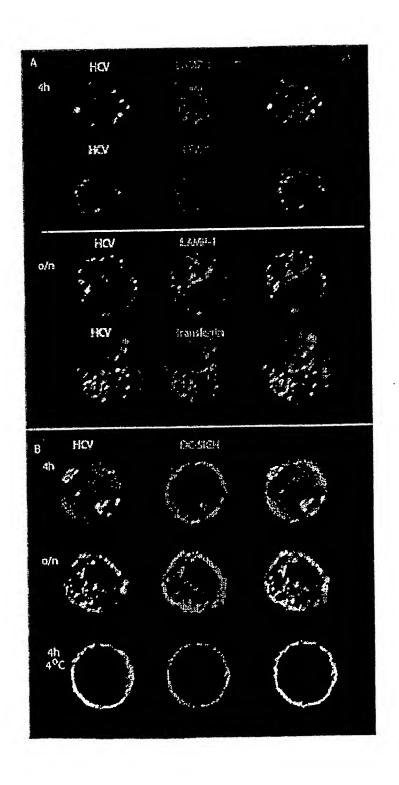


Fig. 40

Immature DC internalize carbohydrates via DC-SIGN

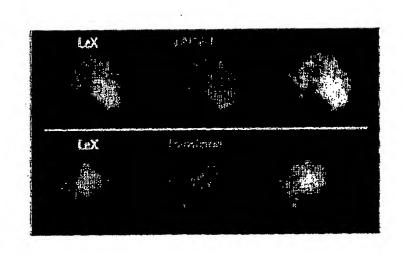


Fig. 41

HCV binding to Liver sections

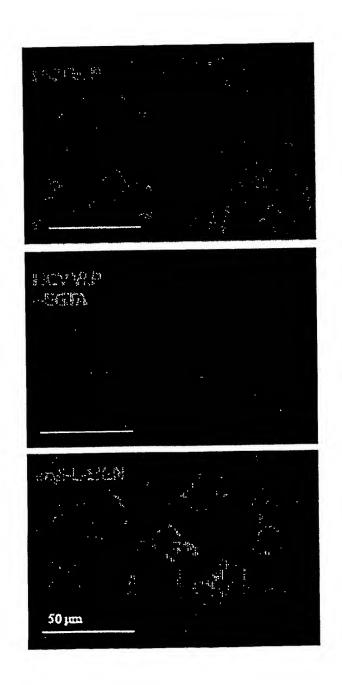


Fig. 42

Lewis blood group antigens and some of their substructures bind to DC-SIGN.

		b 1 2
Structure	Antigen	Lev Lex
		Fuca1-4GIcNAc
Fucα1→ 2Galβ1→3GlcNAc	H type 1	Fuca1-3GIcNAc
, <u> </u>	71	Fucα1-2Galβ
Fucα1→ 2Galβ1→4GlcNAc	H type 2	Fuc
·		Galβ1-3GIcNAc Market Galβ1-4GIcNAc Galβ1-4GIcNAc Galβ1-4GIcNAc Market Galβ1-4GIcNAc Galβ1-4GIC
→3 (Galβ1→4GlcNAcβ1→) _n	L antigen	Gal 📜
•		GlcNAc 🚾
Galβ1→ 4GlcNAc	Lewis x (Le ^x)	H type 1
3		
Fuca 1		OD 490
. 404 !		C 1 2
Fucα1 → 2Galβ1→ 4GlcNAc	Lewis y (Le ^y)	(Lex) ₂
3 ↑		(Lex),
Fuca1		

Fig. 43

Binding of *H. pylori* is dependent on Lewis antigen expression.

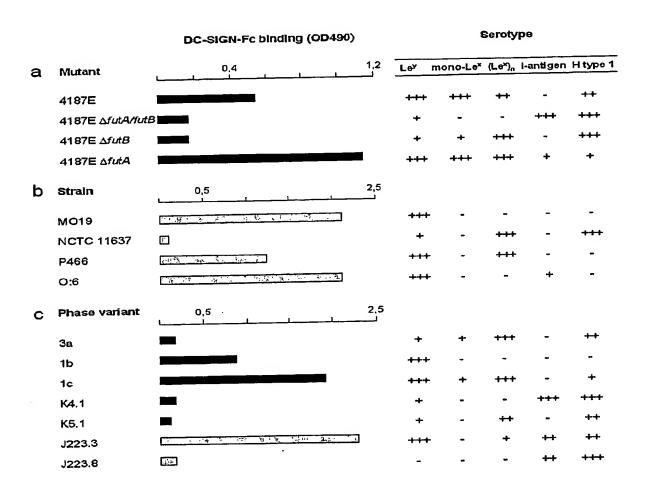


Fig. 44

LPS phase variation in *H. pylori* occurs in vivo.

а	Strain	Number of colonies (%)			•		
			Ley	mono-Lex	(Lex) _n	i-antigen	H type 1
	J223.3	6/30 (20)	+++	•	++	++	+++
	J223.8	24/30 (80)	-	-	•	+++	+++

b	Strain	Length of C	-tract in gene			Serotype	:				
		futA	futB	Ley	mono-Le ^x	(Le _x),	i-antigen	H type 1			
	J223.3	n=9 ("off")	n=10 ("on")	+++	•	++	++	+++			
	J223.8	n=9 ("off")	n=9 ("off")	-	-	-	+++	+++			
	J223.3 ∆futB	N.D.	N.D	•	•	-	+++	+++			

С	J223.3 futA]	J223.3			futB	
	- 7	GAAAGCGCTT	CCCTATTAGA CGCCTTCATA CCATTGAAAA AATGGCCTCT CCCCCTAA (STOP)		1 61	ATGTTCCAAC GAAAGCGCTT AAATCTCCCC	CCATTGAAAA	AATGGCCTCT
	J223.8	8			J223	3.8		
		GAAAGCGCTT	CCCTATTAGA CGCCTTCATA CCATTGAAAA AATGGCCTCT CCCCCTAA (STOP)		1 61		CCCTATTAGA CCATTGAAAA CCCCCTAA (AATGGCCTCT

Fig. 45

DC-SIGN is expressed on gastric DCs and is the major receptor for Le positive *H. pylori*.

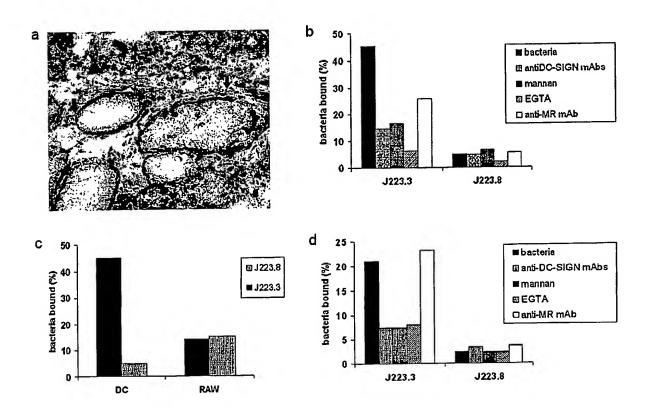
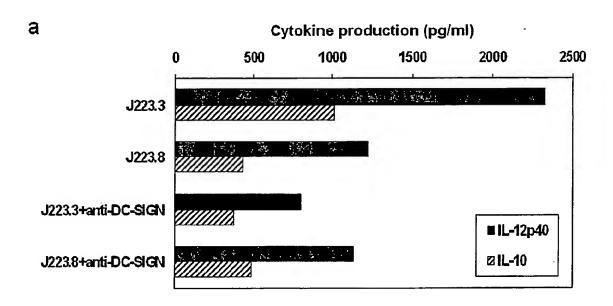


Fig. 46

Binding of *H. pylori* to induces DC-SIGN-dependent increase of IL-10 and IL-12 production, but no changes in IL12p70.



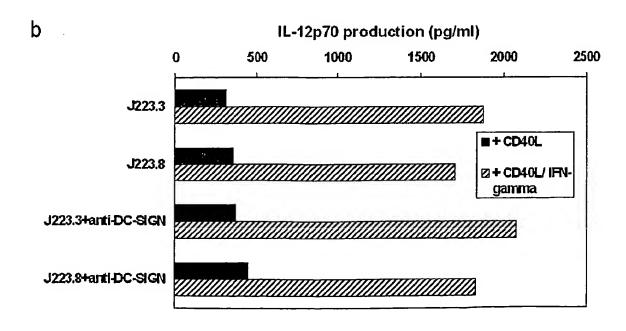
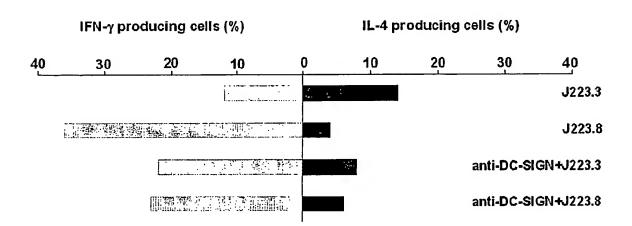


Fig. 47

Binding of *H. pylori* to DC-SIGN induces skewing of naïve T cells to Th2.



Lactobacilli induce partial DC maturation

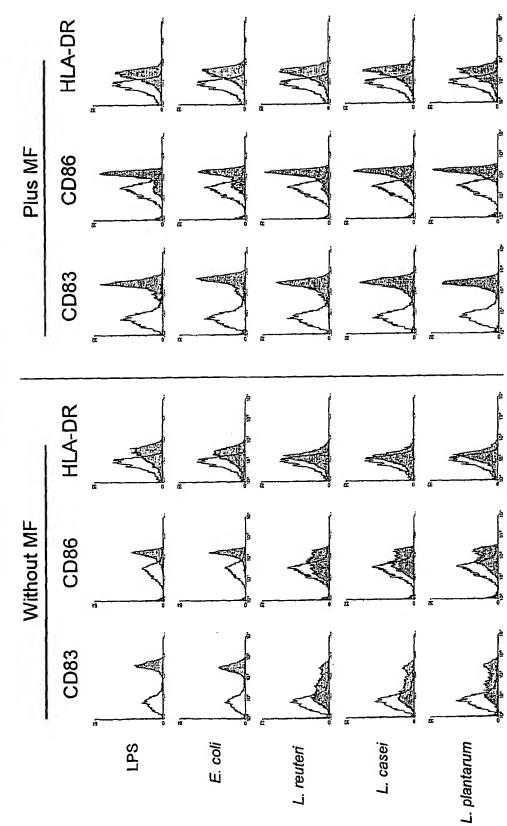


Fig. 48A

Cytokine profiles induced on DC by lactoballi

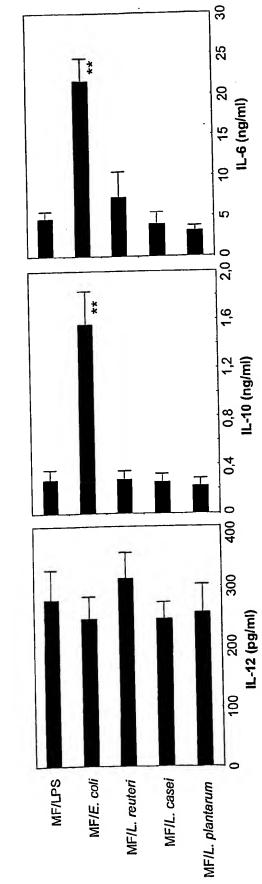


Fig. 48B

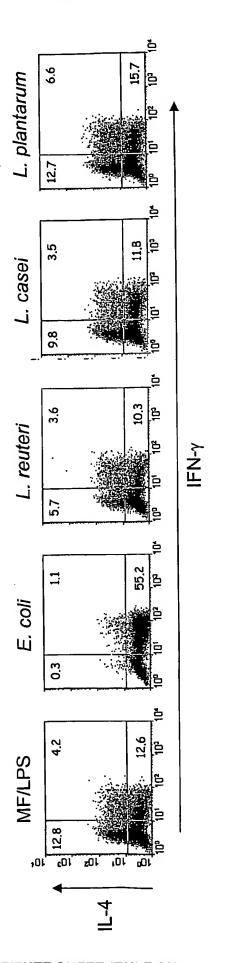


Fig. 49A

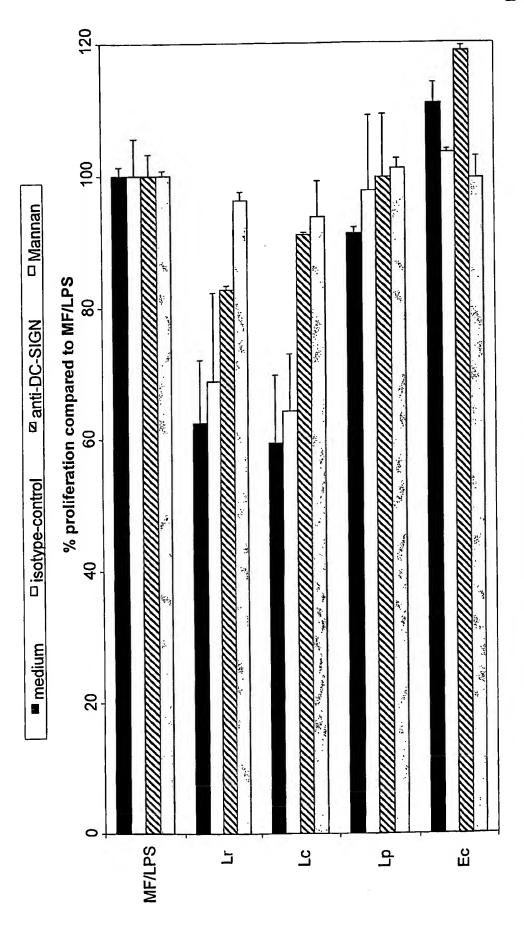
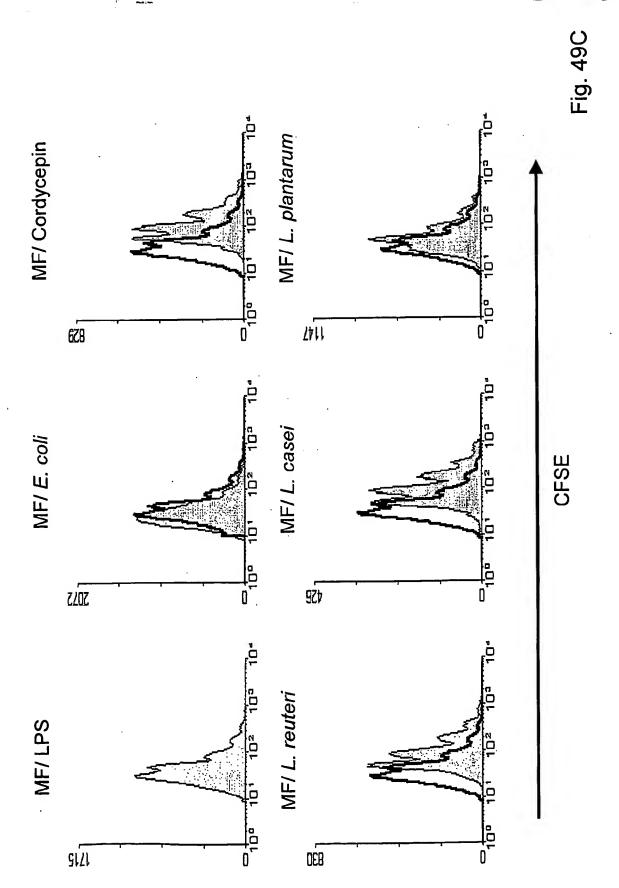


Fig. 49B



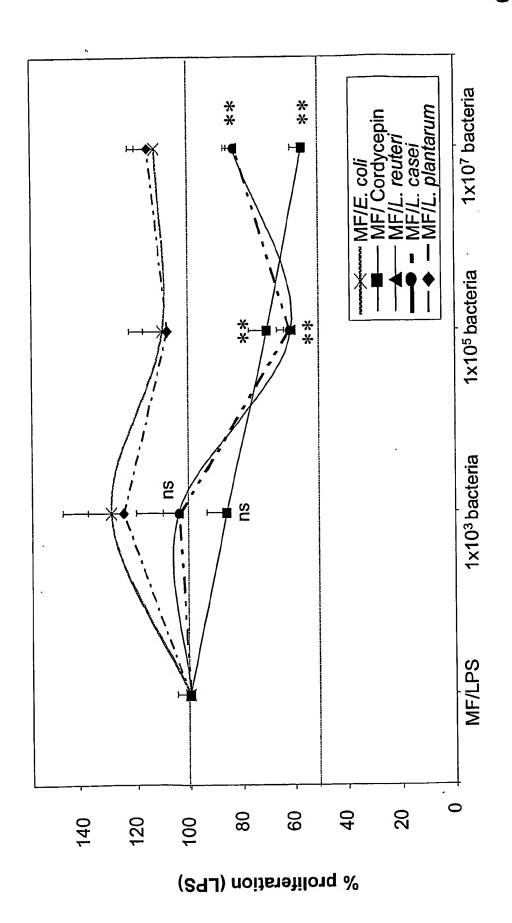
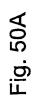
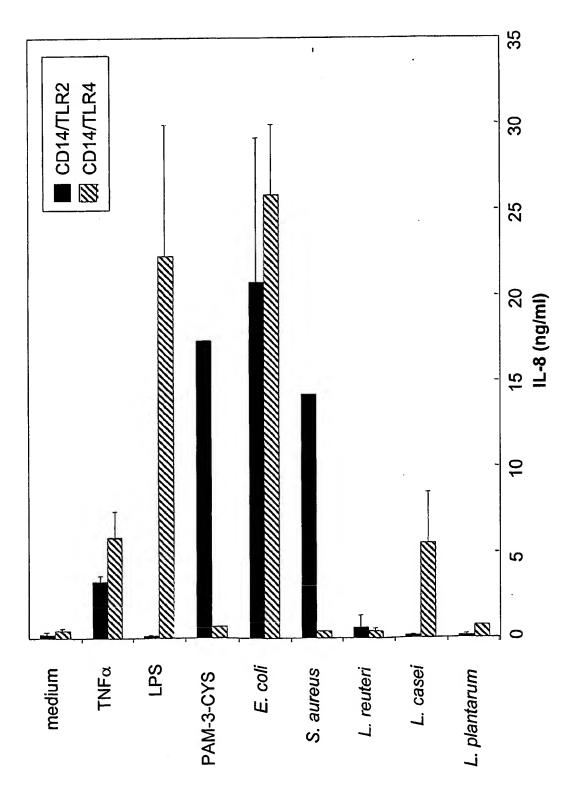
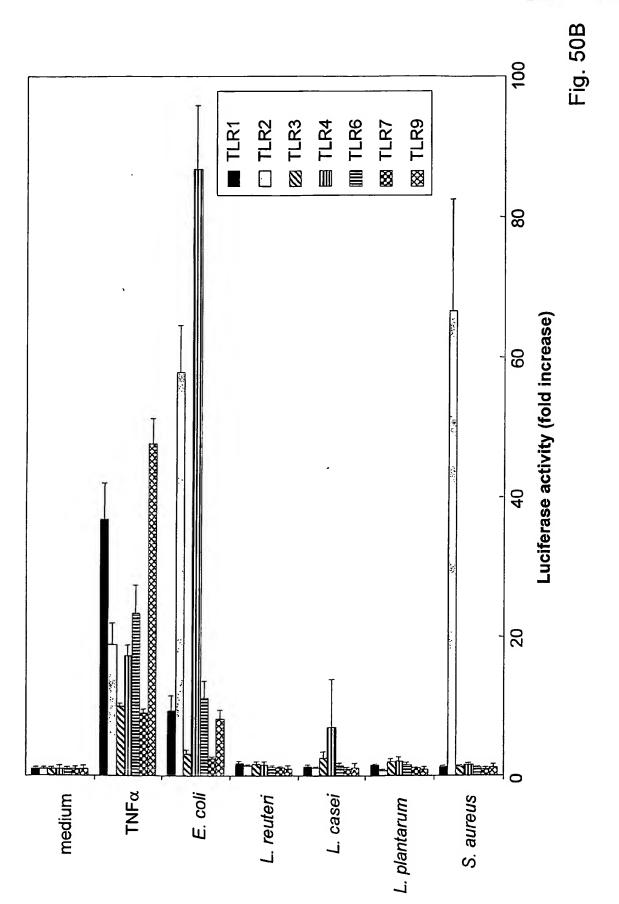
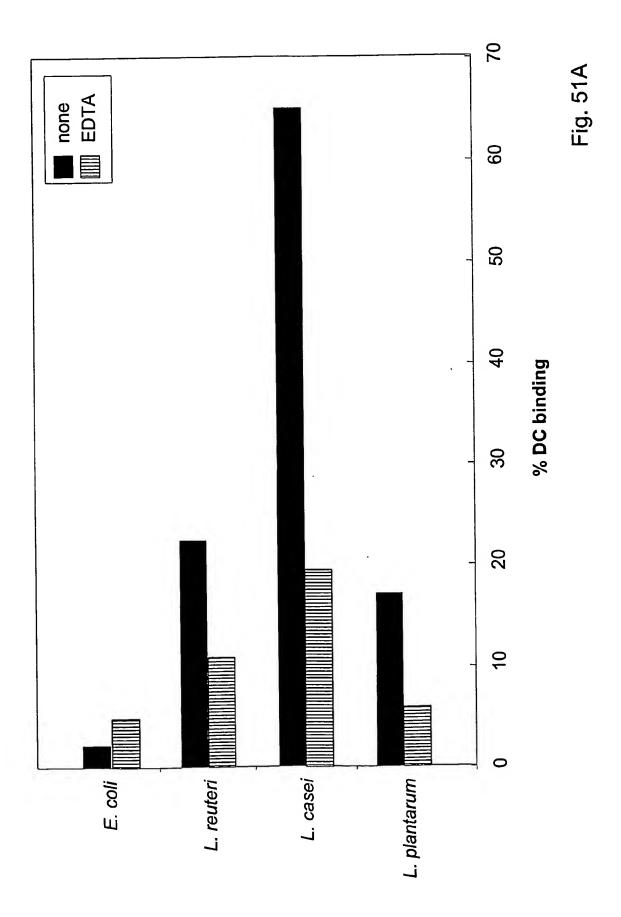


Fig. 49D

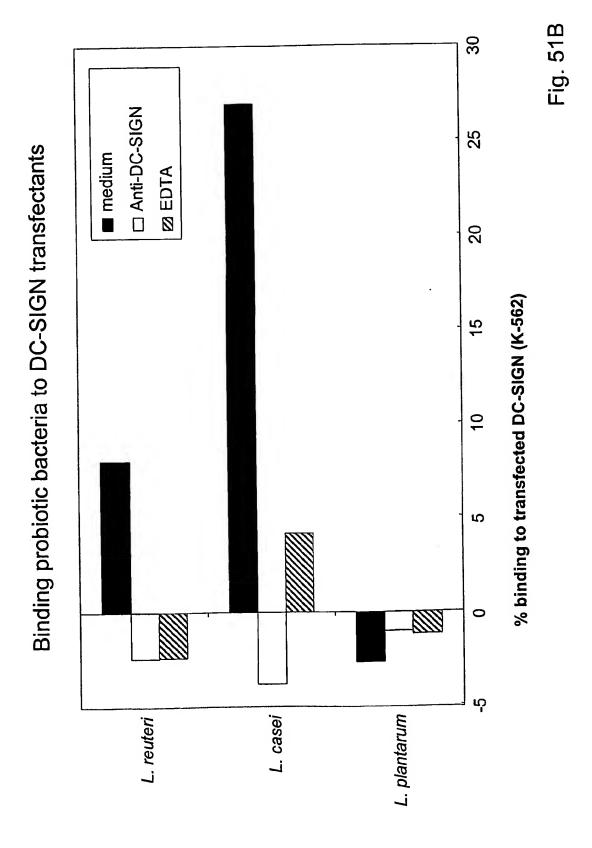


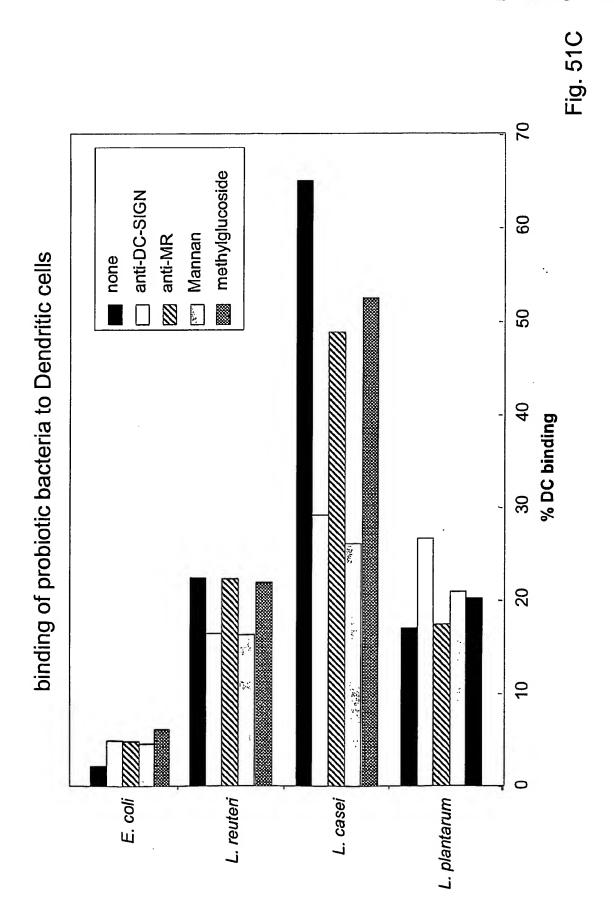






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Induction of T reg cells through targeting DC-SIGN by probiotic bacteria

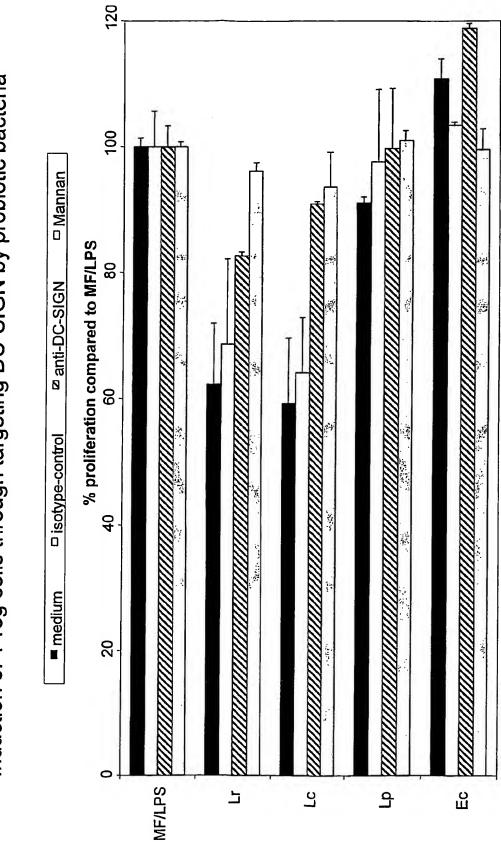


Fig. 52

Fig. 53

PMN express the DC-SIGN ligand Lewis^x and bind with high affinity to recombinant DC-SIGN.

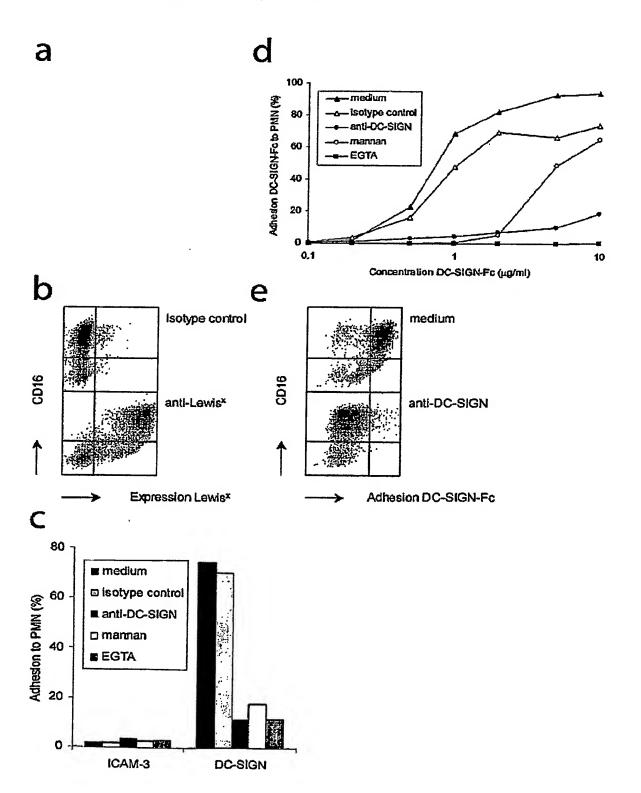


Fig. 54
CEACAM1 expressed on PMN is a ligand of DC-SI

CEACAM1 expressed on PMN is a ligand of DC-SIGN and binds through its Lewis^x moieties.

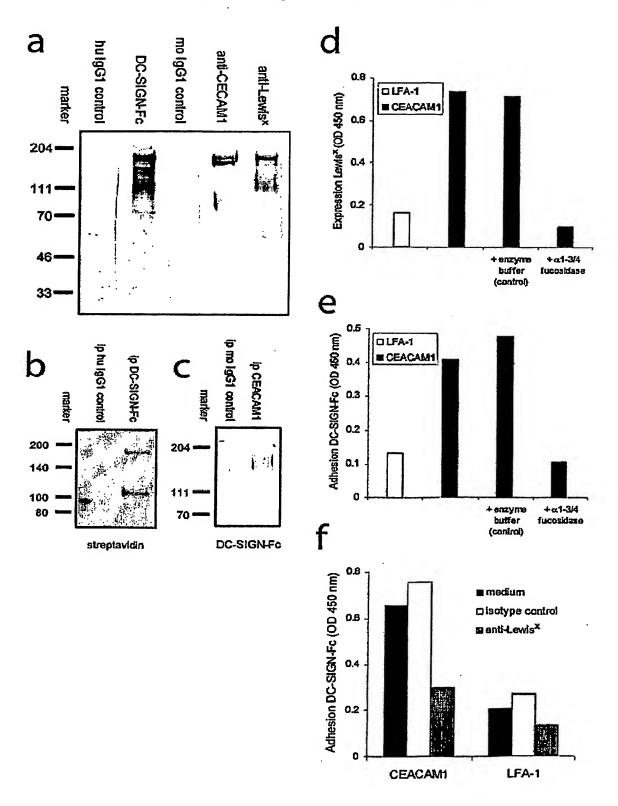
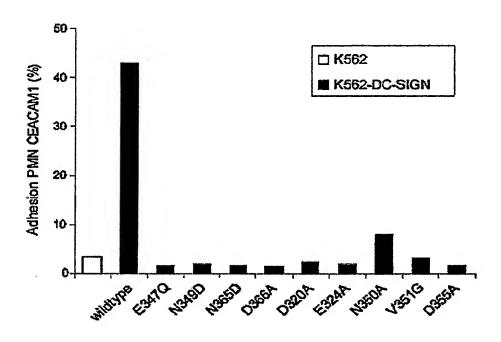


Fig. 55

Cellular DC-SIGN expressed on K562 transfectants and immature DC binds native CEACAM1 from PMN.



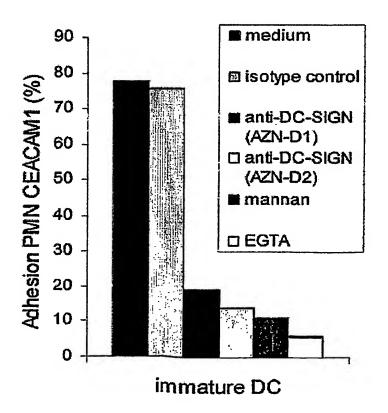
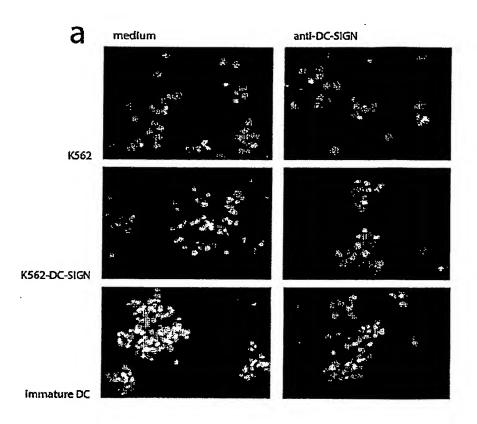


Fig. 56

DC-SIGN is involved in clustering of DC and PMN.



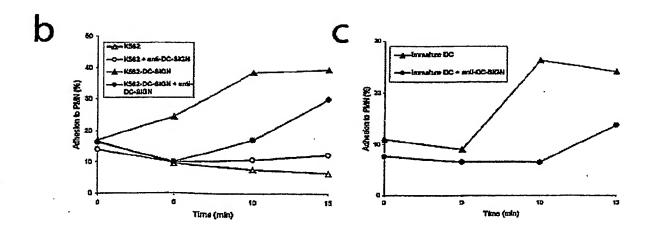


Fig. 57

Localization of PMN and DC in colonic mucosa of patients with Crohn's disease.

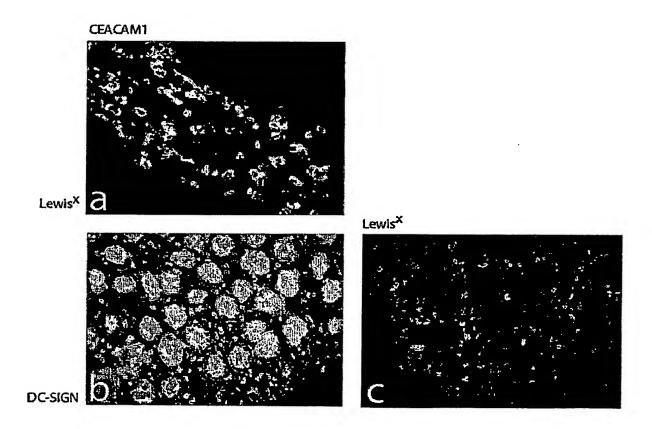
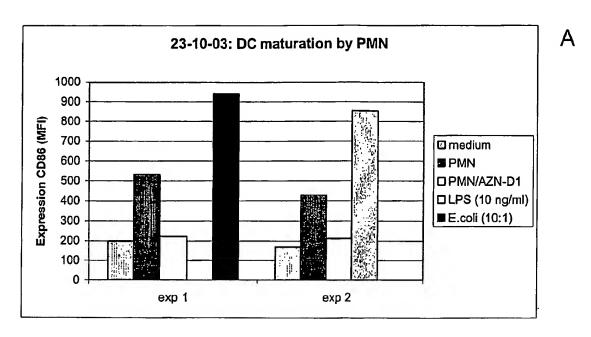
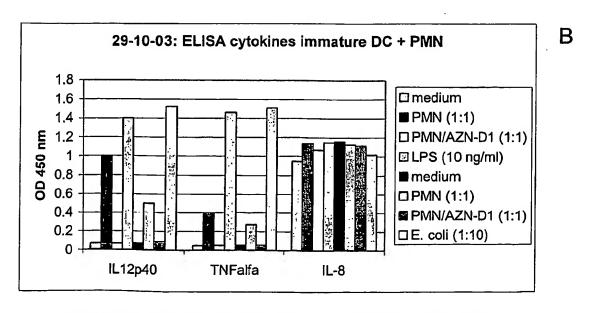


Fig. 58

PMN activate immature DC through binding DC-SIGN.



PMN induce upreguation of co-stimulatory CD86 on DC, which is dependent on DC-SIGN binding



PMN induce secretion of inflammatory cytokines by DC, which is dependent on DC-SIGN binding

Fig. 59

DC-SIGN binds Lex expressing CD11b present on neutroph

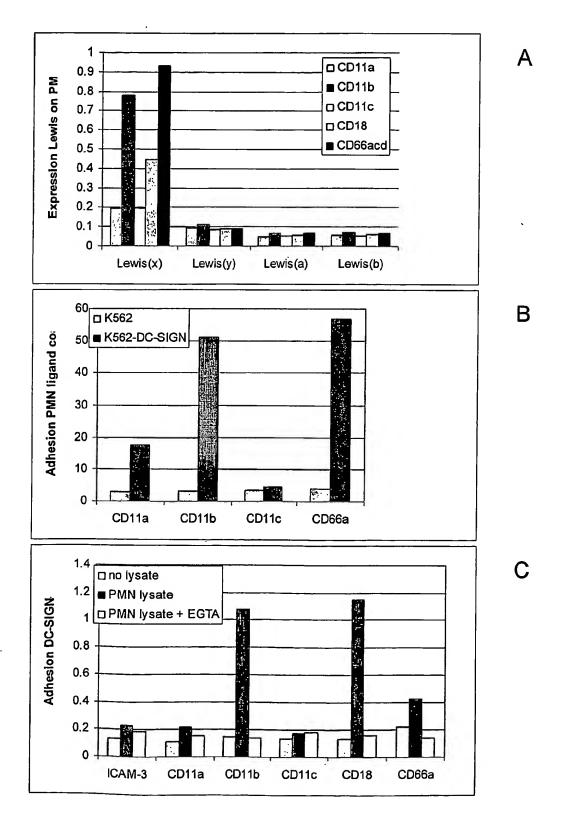
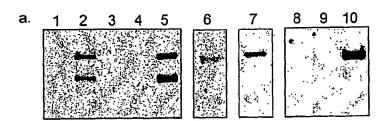


Fig. 59D

DC-SIGN bindsCD66acd and CD11b on PMN



. Biotinylated PMN:

- 1. IP ICAM-3-Fc, IB streptavidin,
- 2. IP DC-SIGN-Fc, IB streptavidin,
- 3. IP anti-DC-SIGN, IB streptavidin,
- 4. IP anti-CD66acd, IB streptavidin,
- 5. IP anti-CD11b, IB streptavidin,
- 6. IP DC-SIGN-Fc, IB anti-CD66acd,
- 7. IP DC-SIGN-Fc, IB anti-CD11b,
- 8 IP anti-DC-SIGN, IB DC-SIGN-Fc,
- 9. IP anti-CD66acd, IB DC-SIGN-Fc,
- 10. IP anti-CD11b, IB DC-SIGN-Fc.
- IB, immunoblotting (detection/binding)
- IP, immunoprecipitation (capture)

10/533989

Fig. 60

DC-SIGN binds Lewis on CD11b



Biotinylated PMN, IP anti-CD11b, IB streptavidin:

- 1. control
- 2. PNGaseF

Biotinylated SW948, IP anti-CD11b, IB DC-SIGN-Fc

- 3. control
- 4. PNGaseF

Biotinylated PMN, IP anti-CD11b, IB streptavidin:

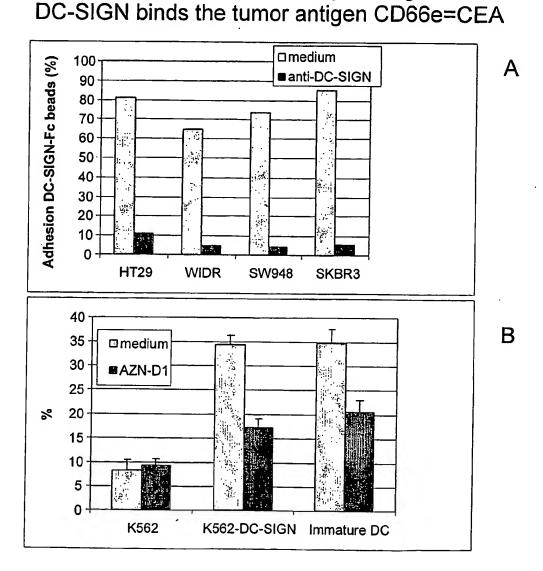
- 5. control
- 6. α -1,3/4-Fucosidase

Biotinylated PMN, IP anti-CD11b, IB DC-SIGN-Fc

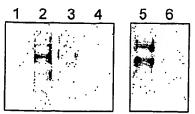
- 7. control
- 8. α -1,3/4-Fucosidase
- IB, immunoblotting (detection/binding)
- IP, immunoprecipitation (capture)

Fig. 61

DC-SIGN binds tumor cells expressing CD66e



1 2 3 4

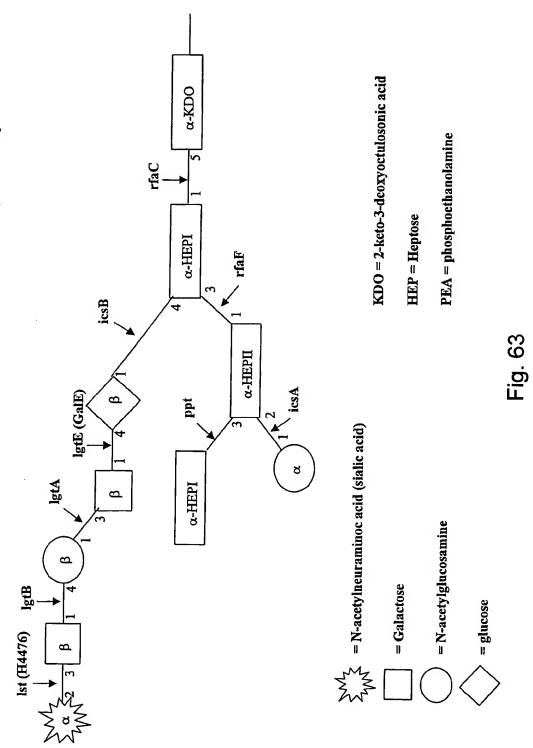


- b. Biotinylated SW948:
- 1. IP ICAM-3-Fc, IB streptavidin,
- 2. IP DC-SIGN-Fc, IB streptavidin
- 3. IP anti-CD66ae, IB streptavidin
- 4. IP anti-CD11b, IB streptavidin
- 5. IP anti-CD66ae, IB DC-SIGN-Fc
- 6. IP anti-CD11b, IB DC-SIGN-Fc
- IB, immunoblotting (detection/binding)
- IP, immunoprecipitation (capture)

Biotinylated SW948, IP anti-Biotinylated SW948, IP anti-CD66a&e, IB streptavidin: CD66a&e, IB DC-SIGN-Fc $\mathbf{\omega}$ 2. α-1,3/4-Fucosidase 4. α-1,3/4-Fucosidase SW948 lysate СD66е DC-SIGN recognizes Le^x-Le^y on CD66e on tumor cells □ no lysate 1. control 3. control CD50 (lgG2b Isotype) СБ66а&е 4 CD11a (lgG1 isotype) 1.2 ö Adhesion DC-SIGN-Fc (OD 450 nm) Fig. 62 Lewis(b) GCD11a (lgG1 isotype) DC-SIGN-Fc ■CD66a&e Lewis(a) Lewis(y) ICAM-3-Fc □ CD66a&e Lewis(x) 0.35 0.25 0.2 Expression Lewis on SW948 (OD 450 nm) Adhesion CD66a&e(OD 450 nm) 4 C

SUBSTITUTE SHEET (RULE 26)

Neisseria meningitis-GlcNAc specificity



Binding of Neisseria Meningitidis to 293T transfectants (100703)

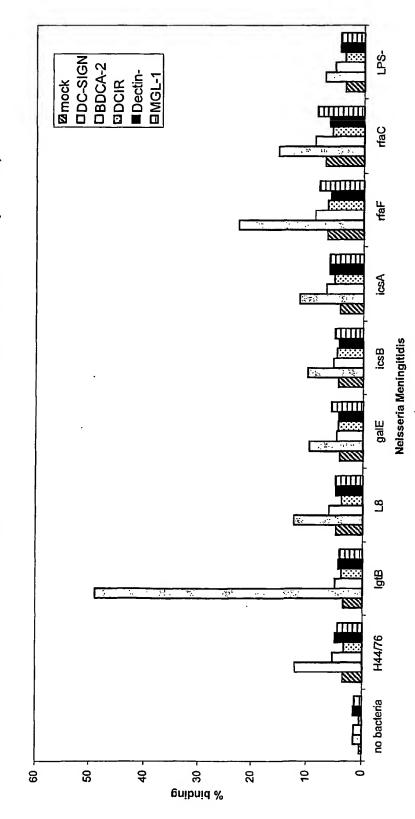


Fig. 62

Binding of Neisseria Meningitidis to DCs (100703)

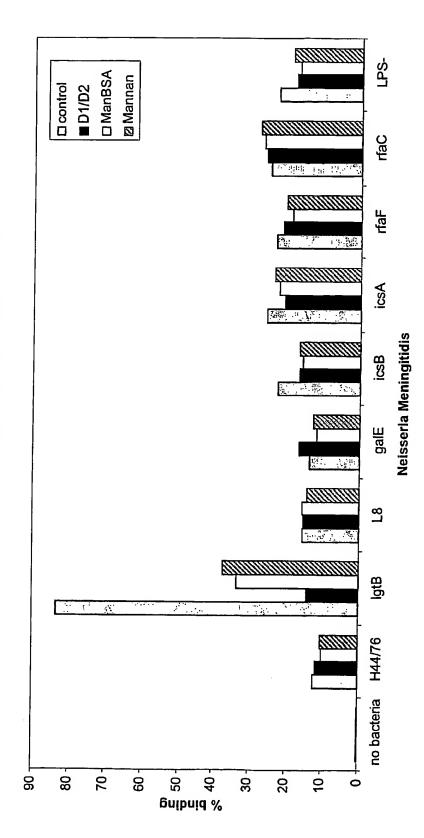
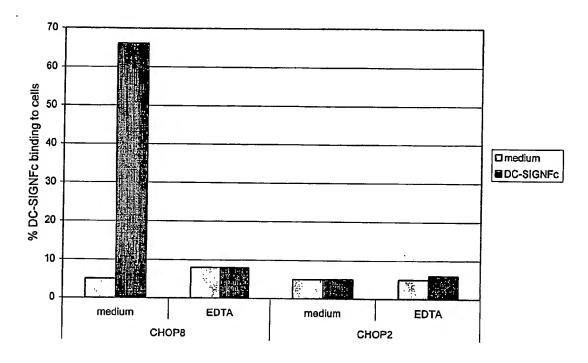


Fig. 65

Fig. 66

DC-SIGNFc binds GlcNAc expressing CHOP8 cells



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